

Myocardial infarction is the result of atherosclerosis of the coronary arteries, and currently there is no cure for atherosclerosis and little hope of retarding its progress. However, much work has gone into the reduction of its complications as there is no specific therapy for the disease itself.

Myocardial infarction is responsible for about 30% of all deaths in the United States. In the past few years, the incidence involving the young has increased at a faster rate than in the older sections of the population.

A study in the U.S.A., the Framingham study, has shown that more than half of those who die from acute myocardial infarction do so within one hour, and only just over half of those with an initial attack of acute infarction survive to hospital. This high frequency of sudden death emphasizes the importance of preventing the development of ischaemic heart disease.

"RECENT ADVANCES IN THE TREATMENT
of
MYOCARDIAL INFARCTION"

In the treatment of myocardial infarction, the immediate prognosis depends on age, sex, previous history, the degree and severity of shock, the presence and severity of heart failure, cardiac rhythm, and the nature and extent of the E.C.G. changes.

by

Affra M. Varcoe-Cocks.

The mortality in myocardial infarction rises with age, and the mortality over 65 years of age is 50-60% or more, and double that in the 45-65 age group. The total number of cases in relation to sex is small, particularly in the younger age groups, women under 65 having higher mortality than men under 65, but the rise in mortality is less steep, so that at age 75 or over the rates are approximately the same for both sexes.

Factors in the previous history to be considered are: (a) previous cardiac infarction, (b) angina pectoris, (c) other abnormal heart findings, (d) other cardiovascular disease, (e) hypertension, (f) diabetes, (g) vascular disease, (h) obesity, (i) smoking. The mortality is 10% in those with a first attack, compared to 30% in those with second attack. Opinions differ as to the prognostic effect of angina. Mortality rates are affected by a rapid dysrhythmia and the presence of heart-



RECENT ADVANCES IN THE TREATMENT OF MYOCARDIAL INFARCTION

Myocardial infarction is the result of atherosclerosis of the coronary arteries, and currently there is no cure for atherosclerosis and little hope of retarding its progression. However, much work has gone into the reduction of its acute cardiac manifestations as there is no specific therapy for acute myocardial infarction.

Diseases of the coronary arteries are responsible for about 30% of all deaths among middle-aged men and it is increasing, the increase involving those under 45 years at a faster rate than in the older sections of the population.

A study in the USA, the Framingham study has shown that more than half of those who die from acute myocardial infarction do so within one hour, and only just over half of those with an initial attack of acute infarction are admitted to hospital. This high frequency of sudden death emphasises the importance of preventing the development of ischaemic heart disease.

It would perhaps be appropriate to discuss here the factors involved in determining the severity of infarction and hence the prognosis of the patient.

Important factors covering the immediate prognosis (1-4 weeks) are age, sex, previous history, the degree and severity of shock, the presence and severity of heart failure, cardiac rhythm, and the nature and extent of the e.c.g. changes.

The mortality in men rises with each quinquennium from 40 to 65, the mortality over 65 being double that in 60-to 64 group, and treble that in the 55 to 59 quinquennium. The total number of women in relation to men is small, particularly in the younger age groups, women under 65 having higher mortality than males under 65, but the rise in mortality is less steep so that at ages of 65 or over the rates are approximately the same for both sexes.

Factors in the previous history to be considered are a) previous cardiac infarction, b) angina without other abnormal cardiovascular findings, c) other cardiovascular including hypertension, peripheral vascular disease, cerebro-vascular disease, cor pulmonale, valvular disease and arrhythmias, and d) exertional dyspnoea. The mortality is 18% in those with first attack, compared to 30% in those with second attack. Opinions differ as to the prognostic effect of angina. Mortality rates are affected with cardiac hypertrophy and the presence of hyper-

tension. It has been suggested that a history of exertional dyspnoea has an adverse effect on mortality rates from myocardial infarction.

It is generally agreed that shock is one of the most important factors influencing mortality in this condition. Shock may be divided into four grades: a) no shock, b) mild and transient shock where the shock develops at or soon after the onset of the attack and it is manifest by transient pallor, faintness, sweating, nausea or vomiting subsiding within 15-30 minutes, c) moderate shock where the signs of shock are still present on examination but subside with rest and sedation, and d) severe shock where the shock persists despite rest and sedation. The mortality is 12% in those with no shock as compared to 33% in those with shock. In the mildly shocked group there is no increase in the overall mortality, but this group is associated with unexpected deaths. Mortality in the moderately shocked group is 38%, and those with severe shock carry a grave prognosis with an 83% mortality.

Signs of cardiac failure in infarction area associated with a high mortality, this applies to congestive cardiac failure as well as left ventricular failure. The mortality in those with failure is 43% compared to 10% in those with no failure

Mortality rates are increased in the presence of arrhythmias with the possible exception of extrasystoles. Atrial fibrillation is classed with atrial flutter and ventricular tachycardia as a sign of extensive infarction. Heart block when partial is not unfavourable, but when complete it is a bad prognostic sign. Persistent sinus tachycardia is also of grave prognostic significance.

The factors considered above may be awarded marks so forming a prognostic index whose value may lie anywhere between 1 and 28. This numerical method allows one to assess the severity and immediate prognosis in those with infarction. In patients who survive the acute stage of the illness the index assessed in the early stage gives a good indication of the average survival time, and for each index range there is a standard mortality: 3% in the 1-8 range, 12% in 9-12, 24% in 13-16, 54% in 17-20, and 88% in the 20+ range.

This index also takes into account the differences in composition of patients falling into individual index ranges, so that conclusions regarding the efficacy of some particular form of treatment can be drawn, and a valid comparison between any two groups of cases can be made. The survival rate at the end of the first year diminishes as the index increases.

As stated above shock is an important factor in myocardial infarction, in particular severe or "cardiogenic shock", which is characterised by a systolic pressure remaining below 80mm.Hg., associated with pallor, cyanosis, sweating, a cold skin and oliguria.

The primary effect in cardiogenic shock is the impairment of the heart as a pump: there is an absence of the reflex increase of systemic vascular resistance of sufficient magnitude to compensate for the severe reduction in cardiac output and to maintain the blood pressure. Factors thought to be involved in the impairment of this reflex are severe acidosis and hypoxia, or injury to the myocardium being responsible for the lack of vasoconstriction by neurogenic or humoral influences. The metabolic acidosis may cause direct depression of myocardial function and diminished pressor response to adrenaline and noradrenaline. Both effects may be reversed by correction of the acidosis by sodium bicarbonate.

There is a severe degree of arterial hypoxaemia in this group of patients. In one study it was found that the administration of oxygen in high concentration failed to cause striking increase in the arterial blood oxygen tension. This variability in the circulatory response to oxygen in the presence of cardiogenic shock was thought to be due to shunting of about 25% of the cardiac output through vessels inaccessible to pulmonary gaseous exchange.

If arterial hypoxia and acidosis in cardiogenic shock are responsible for the diminished sensitivity of both heart and peripheral circulation to sympathetic outflow and the increased levels of circulating catechol amines, the adequate correction of these factors might be of use in reducing mortality. The correction of the acidosis involves careful titration of required amount of buffering solution against serial acid-base determinations in these patients. The value of continuous monitoring is indicated here. Adequate correction of arterial hypoxaemia is a more difficult problem. If the cause of the relative unresponsiveness to high oxygen levels could be determined, tissue hypoxia could be improved and metabolic acidosis avoided. Some authorities may resort to the use of hyperbaric oxygen.

In cardiogenic shock the cardiac output and venous return are reduced, the arterial pressure is low and the peripheral resistance is high owing to the vasoconstriction. Work done by Bloch et al gave some information as to whether lives could be saved in cardiac shock by treatment aimed at increasing the peripheral blood flow. Encouraging results were obtained with the use of phenoxybenzamine, an anti-adre-

nergic vasodilator, and low molecular weight dextrans(LMWDs).

Phenoxybenzamine is a long acting blocking agent which selectively blocks the excitatory response of smooth muscle and exocrine glands to adrenaline and noradrenaline, leaving intact the inhibitory response of smooth muscle and myocardium to adrenaline and related agents. It is known to act specifically on the alpha-adrenergic cells in a non-competitive manner decreasing or abolishing the receptiveness to sympathomimetic stimulus.

LMWD reduces blood viscosity and increases the effective circulating blood volume. In a state of myocardial failure in which micro-circulatory perfusion is reduced, the viscosity of the blood is preponderantly determined by the aggregability of the formed elements and to a lesser extent by the properties of the plasma. Theories on its action are a) that it decreases viscosity of slowly flowing or suspended elements in blood by coating the blood cells with an enhanced electronegative charge so increasing their mutual repulsion, and b) that the antiviscous effect may be attributed to physical protection by coating the cells with a dextran film. When these solutions are infused the effective circulating blood volume is increased not only by the volume of the added fluid but by a secondary volume of extracellular fluid drawn into the intravascular space to maintain isosmolarity.

The benefit of both phenoxybenzamine and LMWD can thus be ascribed to increased peripheral perfusion, the former acting on constricted vessels and the latter on the blood.

At present trials are in progress to determine the use of the drug propranolol. The actions of the drug are to reduce the cardiac output and ventricular contractility, to produce a more economical use of oxygen and it is effective in suppressing and correcting certain arrhythmias.

Propranolol produces beta-adrenergic blockade which increases exercise tolerance a) by inhibiting tachycardia so allowing a longer diastole and a greater coronary blood flow, and b) it reduces contractility and therefore allows a more efficient utilization of the oxygen available. Sympathetic stimulation increases myocardial contractility and oxygen consumption, while reduction of sympathetic drive by beta-blockage reduces these factors.

As mentioned above, propranolol also inhibits some arrhythmias and slows the rate or shortens the duration of others. Part of this effect

may be attributable to beta-adrenergic blockade, but in addition it almost certainly has anti-arrhythmic action which is independent of its ability to inhibit beta-receptors.

Those conditions in which beta-blockade is found to be effective include atrial fibrillation, atrial flutter, ventricular tachycardia, ventricular premature beats and ventricular fibrillation. The potential importance of such an effect can be judged from the recent findings of Julian et al who found by continuous monitoring that some disturbance of rhythm occurred in 95% of patients in the acute stage of myocardial infarction.

The effectiveness of the drug in controlling or inhibiting these arrhythmias cannot be established without continuous e.c.g. monitoring of treated and control groups of patients.

In recent years external electrical defibrillation has been developed. The incidence of ventricular fibrillation is 70% in myocardial infarction. There are two methods of defibrillation; by the use of drugs or by electrical means. The latter has superseded the former due to its superiority in the management of fibrillation.

The basic principle is the simultaneous depolarization of all fibres of heart muscle, so that they are all in the refractory period at the same time and hence in a condition suitable for the normal beat to commence. Depolarization is produced by passing a large current through the heart for a short time. Two types of current may be used, either alternating or direct current. Alternating current was the first type to be used, but direct current has been found to be more effective in stopping ventricular fibrillation, and to do less damage to the heart.

Various methods of cardiac pacing have been developed, the four main types being: a) epicardial electrodes with an external pacemaker, b) intracardiac electrodes with an external pacemaker, c) epicardial electrodes with an implanted pacemaker, and d) intracardiac electrodes with an implanted pacemaker. The method used will depend on the case under consideration. Complications seem to be either of infection tracking along the electrode leads, or of a psychological nature, particularly where external leads are used and the patient is constantly being reminded of his precarious condition.

After complete occlusion of a coronary artery the resting diastolic polarization of the myocardial fibres in the area supplied by the occluded vessel is reduced. The degree of diastolic polarization varies in the different zones of the infarcted area and determines whether the zone is completely unexcitable (dead zone), or is activated

with a delay (injury zone), or represents only alterations on its recovery or repolarization (ischaemic zone). The dead zone is identified electrocardiographically by Q waves or QS complexes, the injury zone by displacements of the RS-T segments and the ischaemic zone by T wave inversion.

All differences of membrane potential have their source in the uneven distribution of organic ions on the two sides of the membrane.

The concentration of K inside the fibre (K_i) is about thirty times higher than that outside the fibre (K_o). The concentration of other ions in the extracellular fluid exerts little or no effect on the transmembrane potential.

In infarction there is a decrease in the K_i/K_o gradient because of a decreased K_i , and it was thought that a physiologic approach to treatment might modify the altered gradient by forcing the potassium into the fibres. It was also thought that the energetic mechanism underlying potassium movements across the membrane could be improved. Such a response can be obtained through a combined administration of potassium, glucose and insulin.

Study of this treatment on the e.c.g. changes in myocardial infarction showed that the e.c.g. signs were modified. It was also observed that there was an absence or prompt disappearance of arrhythmias, a sense of well-being by the patient and the relief of their pain.

The mechanism of action of potassium, glucose and insulin treatment is thought to be as follows. Insulin decreases the serum potassium concentration by increasing the potassium uptake by liver, skeletal and cardiac muscles, and accelerates the transport of glucose across the cell membrane. By increasing the intracellular accumulation of glucose and potassium the process of oxidative phosphorylation and transfer of high energy phosphate is enhanced. Intravenous administration of potassium results in storage mainly by the heart, and through the effect of insulin the intracellular potassium in the heart is increased.

The above experimental advances in the management of infarction require more observation in units which are specially equipped and where intensive care of the patients can be undertaken.

The concept of special care units for patients with acute myocardial infarction first arose from the recognition that 60% of deaths in these patients occur in the first week. Sudden deaths from cardiac arrest are common in this period. With the development of

external cardiac massage, external electrical defibrillation and external electrical pacing continuous electrocardiographic monitoring was developed with a view to the immediate detection and correction of ventricular fibrillation and asystole. This monitoring has also led to the conclusion that abnormalities of conduction and ~~excitation~~ occur in 90-95% of patients with infarction.

At present there are ~~a~~relatively few coronary care units, but in those that have been operating it is thought that with special staff and equipment these units should ~~result~~ result in reduction of mortality through immediate effective resuscitation of patients following cardiac arrest, through the rapid conversion of arrhythmias to normal rhythm, possibly through the earlier control of hypotension, cardiac failure and cardiogenic shock ~~and~~ perhaps their prevention.

Proper staffing of a unit entails a sister being on duty at all times with a roster of medical staff on call. Equipment consists of respirator and resuscitator connected to a face mask ~~y~~ to deliver oxygen from piped wall supply, a defibrillator and external/internal pacemaker. All drugs likely to be required for cardiac emergencies should be kept in the unit, and facilities for tracheal intubation and tracheostomy should be available.

The patient is connected by chest electrodes to an e.c.g. recorder, cathode-ray oscilloscope, heart rate meter and a rate activated alarm. An automatic recorder may be activated when a predetermined variation in heart rate persists for more than, for example, 8 seconds.

Important in determining the outcome of a patient ~~and the~~ severity of the infarct as judged by the haemodynamic ~~effects~~ effects of the infarct. There is a natural tendency to admit to these units the patients who are most severely ill after the infarct, but results of one study suggest that monitoring with a view to the detection and correction of cardiac arrest should be preferred for patients with the least circulatory embarrassment. A lot of controversy over these units centres around the methods of selection of patients .

Ventricular fibrillation tends to be the cause of cardiac arrest in the milder cases, asystole occurring in the more severely ill patients with cardiac failure and cardiogenic shock. Asystole complicating myocardial infarction is thought to be of more grave prognostic significance than is ~~ventricular~~ ventricular fibrillation. Recurrent ventricular fibrillation is likely to occur in previously resuscitated patients if the ~~infarct~~ infarct is severe, and studies have shown that

propranolol may be of better use than procainamide and quinidine. Recurrence of asystole in patients with complete atrioventricular block or following resuscitation from an initial episode is also frequent, and here internal catheter electrode pacing appears to have a place.

Several studies have therefore shown that coronary care units are important factors in reducing mortality from myocardial infarction. It is considered that all patients with an infarct should be admitted to the unit for the first four to five days, and that in patients with cardiac failure and serious arrhythmias continued special care is required for two to three weeks from the onset of the infarct to reduce later deaths.

Because of the frequency of sudden but not irreversible collapse of the circulatory system, for example, from myocardial infarction there have been numerous attempts to substitute the heart temporarily. These methods include cardiopulmonary bypass, left heart bypass, venoarterial pumping and aortic counterpulsation.

Cardiopulmonary bypass involves the removal of inferior caval blood, its oxygenation and its return to the right brachial artery. However, disadvantages were found including petechial haemorrhages in the area perfused by the returned blood, and the development of haematuria and severe renal damage, and the question was raised as to whether this form of bypass reduced the work of the left ventricle.

The appreciation both of the deleterious effects and the high mortality of prolonged use of the oxygenator and doubt about the reduction of the left heart work led to the study of the possibility of left heart bypass without thoracotomy, and the effectiveness of this method on reducing the metabolic work of the left ventricle. In this method a cannula is placed from left atrium to main pulmonary artery, and it is believed that shortening of the end-diastolic fibre length is the factor which permits a reduction of oxygen utilization.

The question has been raised as to whether manipulation increases the risk of the development of any arrhythmia, but these two methods of cardiopulmonary and left heart bypass appear to give protection against the development of ventricular fibrillation.

In another method, that of veno-arterial pumping, the aim was to increase the systemic pressure and decrease the work of the heart, by sucking the blood from the veins and pumping it into the arteries without oxygenation. This method is simple but has the obvious disadvantage of reducing the saturation of arterial blood.

Aortic counter pulsation is a method of assisting the circulation by reducing the pressure against which the left ventricle contracts while increasing the coronary blood flow. It is accomplished by cannulating a major artery and aspirating arterial blood into a pump during systole, thus reducing the pressure generated by the left ventricle and so its work. The return of this volume of blood during diastole results in an elevated diastolic perfusion pressure and an augmented coronary blood flow. No physiological or pathological changes appear to be produced when the pump and cardiac systoles are properly phased.

These surgical methods of management of myocardial infarction are still in their early experimental stages, and it may be that the answer will lie in total heart replacement of which studies are also being made.

As to the preventive aspect of myocardial infarction, coronary angiography and the study of the aetiology and possible prevention of the development of atherosclerosis may be mentioned.

Various methods of coronary angiography have been devised, in particular by cannulation of the coronary ostia themselves. This, however, offers little aid to the diagnosis of ischaemic heart disease that cannot be obtained from history-taking and e.c.g., but it may have a place when atypical pain makes diagnosis difficult. Selective angiography is essential before direct operation on the coronary arteries, but few patients with ischaemic heart disease have a pattern of coronary atheroma sufficiently confined to permit endarterectomy or grafting. The part played by coronary angiography in the possible treatment of myocardial infarction is small, but it does play a part in the research on myocardial blood flow.

Atherosclerosis begins in childhood and progresses with age. Whether coronary atheroma will lead to ischaemic heart disease is determined by many factors: a) the degree and the site of arterial disease, b) the occurrence and extent of thrombotic occlusion of the arterial lumen, c) the adequacy of the coronary anastomotic circulation, d) the myocardial demands, and e) the anatomical distribution of the coronary arteries.

Prevention depends on the effectiveness with which the causal factors can be controlled. Nothing can be done about the anatomy, and permanent reduction of myocardial demands below a certain threshold is impossible and undesirable. The prevention of coronary atherosclerosis and thrombosis and the improvement of coronary anastomosis may be thought

of as one, as the degree of development of one is closely related to the other.

The identification of those in the population who are most at risk is important for effective prevention. Surveys done show that apparently healthy individuals with the following characteristics or habits have a greater incidence of ischaemic heart disease: hyperlipidaemic states, hypertension, cigarette smoking, physical inactivity, and premature cessation of ovarian activity.

Potentially important influences include diabetes, psychogenic stress, a rapid gain of weight and a thrombotic tendency.

Ischaemic heart disease is likely to result from an interplay of multiple related factors than from one factor.

Hypercholesterolaemia is one of the most important risk factors, probably present in about 20% of the population. Raised serum triglycerides are probably as important as high cholesterol levels.

Recent advances in drugs, for example, clofibrate (AtromidS) and in dietetics have made it possible to lower the level of serum lipids in most patients. One study has shown that in patients with hypercholesterolaemia and ischaemic heart disease the fibrinolytic activity of venous blood is much lower than in the healthy controls, and that there is a close inverse relationship between the level of this activity and of serum cholesterol. In this study the cholesterol level was lowered by treatment with Atromid and the fibrinolytic activity was correspondingly enhanced by it. Another study shows that the fibrinolytic activity of patients with ischaemic heart disease and normal cholesterol levels is within the same range as that of a healthy group of controls. No relation between this activity and levels of serum cholesterol was found. It was thought that these results, if one accepts that decreased fibrinolytic activity plays a part in the pathogenesis of atherosclerosis, may imply that the aetiological factors in the production of atherosclerosis are different in patients with hypercholesterolaemia from what they are in those with normal blood cholesterol levels.

Only large scale long-term studies in those who are asymptomatic will indicate the possible value of Atromid in the prevention of ischaemic heart disease, in particular of myocardial infarction, and these are in progress.

It can be seen that recent advances in the diagnosis and in the medical and surgical treatment of myocardial infarction have overshadowed the preventive approach of the disease, and there can be no doubt that here lies the ultimate answer to the problem.

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